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The role f IL-23 in experimental autoimmune encephalomyelitis.

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It has been previously demonstrated that neutralization of IL-12 can ameliorate autoimmune disease. However, studies primarily targeted the p40 subunit, rather than IL-12p35. Interestingly, IL-12p40 is shared by IL-23, a recently described heterodimeric cytokine. Therefore, it was unclear whether the previous findings were due to IL-12 or IL-23 blockade. In this study, our objective was to differentiate the roles of IL-12 and IL-23 in a model of chronic autoimmune disease, relapsing experimental autoimmune encephalomyelitis (EAE). In a side-by-side comparison, mice were treated with neutralizing monoclonal antibodies specific for either IL-12p35 or IL-12/23p40, after myelin basic protein (MBP) immunization. Antibody concentrations were carefully modified to ensure equivalent in vivo efficacy. Results were analyzed by clinical score analysis, histopathology, in vitro proliferation assays, and cytokine profiles. IL-12 specific neutralization had no beneficial effect on progression of EAE. However, neutralization of both IL-12 and IL-23 effectively ameliorated EAE clinical signs and MBP-specific Th cell responses. These data suggest a dominant role for IL-23 in a model of chronic autoimmune disease.

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